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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,678	04/18/2001	David Ogle		7858

7590 11/13/2003

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EXAMINER	
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ART UNIT	PAPER NUMBER
1753	10

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

CTLO 10

Office Action Summary	Application No.	Applicant(s)	
	09/837,678	OGLE ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6,7,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Objections

1. Claims 5, 19, 29 and 31 are objected to because of the following informalities:

a) Claim 5, line 1: -- volume -- should be inserted between "sample" and "to";

b) Claim 19, line 1: -- volume -- should be inserted between "sample" and "to";

c) Claim 29, line 1: "a least" should be -- at least a --;

d) Claim 31, line 3: -- a – should be inserted between "in" and "second".

2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claim 1, lines 14-15 refers to "a selected separation product" of "a sample constituent." What is the constituent separated into? "[S]ample constituent" already implies a separated component of the sample;

b) Claim 1, line 1 refers to "an apparatus for processing compounds," however; no mention is made of compounds in the body of the claim. Instead, terms such as "a sample constituent" and "a selected separation product" are used;

c) Claims 2-4: what has a small volume(s)? Are the samples in small volumes or the interstitial volumes in the apparatus or something else?

d) Claim 2 recites the limitation "small volume" (singular) in line 1. There is insufficient antecedent basis for this limitation in the claim;

e) Claim 15, lines 15-16 refers to "a selected separation product" of "a sample constituent." What is the constituent separated into? "[S]ample constituent" already implies a separated component of the sample;

f) Claim 15, line 1 refers to "an apparatus for processing compounds," however; no mention is made of compounds in the body of the claim. Instead, terms such as "a sample constituent" and "a selected separation product" are used;

g) Claims 16-18: what has a small volume(s)? Are the samples in small volumes or the interstitial volumes in the apparatus or something else?

h) Claim 16 recites the limitation "small volume" (singular) in line 1. There is insufficient antecedent basis for this limitation in the claim;

i) Claim 28, lines 15-16 refers to "a selected separation product" of "a sample constituent." What is the constituent separated into? "[S]ample constituent" already implies a separated component of the sample;

j) Claim 28, line 1 refers to "an apparatus for processing compounds," however; no mention is made of compounds in the body of the claim. Instead, terms such as "a sample constituent" and "a selected separation product" are used;

k) Claim 33 recites the limitation "selected salts in the sample" in line 7. There is insufficient antecedent basis for this limitation in the claim;

l) Claim 33 recites the limitation "the mixture" in line 7. There is insufficient antecedent basis for this limitation in the claim;

m) Claim 33 recites the limitation "at least one compound" in line 9. There is insufficient antecedent basis for this limitation in the claim;

n) Claim 34 recites the limitation "selected salts in the sample" in lines 9-10. There is insufficient antecedent basis for this limitation in the claim;

o) Claim 34 recites the limitation "at least one compound" in line 12. There is insufficient antecedent basis for this limitation in the claim; and

p) Claim 34 recites the limitation "the mixture" in line 10. There is insufficient antecedent basis for this limitation in the claim.

4. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-3, 5-10, 12-17, 19-24, 26-30, 32, 35, and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Speicher et al. (US 6,638,408 B1).

Addressing claim 1, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (see the abstract and col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between a selected one of the cathode buffer zone and the anode buffer zone and the first barrier so as to define a first interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone and the anode buffer zone, a sample constituent is provided to the first interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent through a selected one of the first and second separation barriers, and provided to a selected one of the cathode buffer and anode buffer zones; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones or the first interstitial volume

(anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

Addressing Claims 2 and 16, it will be first noted that sample volume is only intended use. In any event, a sample volume less than about 5 ml is implied by col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml.

Addressing Claims 3 and 17, it will be first noted that sample volume is only intended use. In any event, a sample volume within the range of up to about 2 ml is implied by col. 7, ll. 12-17, which teaches each compartment having a volume of preferably less than 2 ml.

Addressing claims 5-8 and 19-22, these claims only provide intended uses that do not structurally further limit the invention of claim 1. Since no specific sample volume, which is an intended use, is required by any of these claims, the barrier surface area is not limited. Thus, the rejection of claim 1, above, also applies to claims 5-8.

Addressing claims 9, 10, and 24 as seen in col. 4, ln. 55 – col. 5, ln. 54, especially col. 5, ll. 44-46, the Speicher et al. reference discloses various separation barriers, which are electrophoresis membranes, including a membrane made of polyacrylamide that is permeable to small ions and has a molecular weight cut-off of 1kDa.

Addressing Claims 12 and 26, dialysis membranes are disclosed in col. 5, ll. 53-54, for example.

Addressing claims 13 and 27, although the Speicher et al. reference does not mention whether "the first and second separation barriers are adapted to be removed from the apparatus," that the membranes are so adapted is implied by col.16, ll. 48-50, which teaches that the membranes may be removed so that molecules trapped in them can be eluted.

Addressing claim 14, "a plurality of separation barriers spaced apart defining a plurality of interstitial volumes" is shown in Figure 1. Also see col. 6, ll. 57-61, which teaches providing 100 or more separation barriers.

Addressing claim 15, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (abstract and col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between the cathode buffer zone and the first barrier so as to define a first interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

(e) a third separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first or second separation barrier) disposed between the anode buffer zone and the first barrier so as to define a second interstitial volume therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone, the anode buffer zone, and at least one of the first interstitial and second interstitial volumes, a sample constituent is provided to a selected one of the first interstitial and second interstitial volumes, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent, through the first separation barrier, and provided to a selected one of the cathode buffer and anode buffer zones; and provided to the other of the first interstitial and second interstitial volumes; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones, the first interstitial volume or the second interstitial volume (anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

Addressing claim 23, two preferred pore sizes are disclosed in col. 5, ll. 62-66. That the membranes at the first and second ends of the apparatus are permeable to ions is disclosed in col. 5, ll. 48-56.

Addressing claim 28, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (abstract and col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between the cathode buffer zone and the first barrier so as to define a first sample interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

(e) a third separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first or second separation barrier) disposed between the anode buffer zone and the first barrier so as to define a first separation interstitial volume therebetween (any of **180**, **185**, **190**, **195**, or **200** not selected as the first sample interstitial volume);

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone,

the anode buffer zone, and at least one of the first sample interstitial and first separation interstitial volumes, a sample constituent is provided to the first sample interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent, through the first separation barrier, and provided to the first separation interstitial volume, and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones, the first interstitial volume or the first separation interstitial volume (anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

Addressing claim 29, at least a fourth separation barrier is shown in Figure 1.

Addressing claims 30 and 32, at least a fifth separation barrier is shown in Figure 1.

Addressing claims 35 and 36, separating a compound in small volumes of solution as claimed is disclosed by Example 7 in column 15, for example. The claim steps of adding anode and cathode buffer, introducing a sample into the apparatus, and applying a voltage potential are clearly necessary in order to use the apparatus for separating a compound in a sample volume.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-11, 14-25, 28-32, 35, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Derwent abstract and Figure 1 of Murakawa et al. (JP 03118462 A) in view of Speicher et al. (US 6,638,408 B1).

Addressing claim 1, the Murakawa et al. reference teaches an apparatus for processing compounds (abstract and Fig. 1), by electrophoretic separation (abstract), the apparatus comprising:

(a) a cathode (**2** in Fig. 1) in a static cathode buffer zone;

(b) an anode (**3**) in a static anode buffer zone, the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode;

(c) a first separation barrier (**5**) disposed in the electric field area;

(d) a second separation barrier (**6**) disposed between a selected one of the cathode buffer zone and the anode buffer zone and the first barrier so as to define a first interstitial volume (**4**) therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone and the anode buffer zone, a sample constituent is provided to the first interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent through a selected one of the first and second separation barriers, and provided to a selected one of the cathode buffer and anode buffer zones; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones or the first interstitial volume (abstract and Fig. 1).

The Murakawa et al. reference does not mention whether the apparatus is configured for small sample volumes. The Speicher et al. reference teaches an apparatus for separating molecules using an electric field, the apparatus having an anode, a cathode, and several separation membranes and when used the apparatus does not circulate the anode buffer, the cathode buffer, or sample constituents. The apparatus of the Speicher et al. reference is clearly configured for small sample volumes as the reference teaches compartments formed by separation membranes each having a volume of less than 5 ml. It would have been obvious to one with ordinary skill in the art at the time the invention was made to scale the apparatus to process a small sample volume as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because this will optimize the apparatus for separations on small sample volumes. In other words, it would have been obvious to scale the apparatus to accommodate a sample volume within the expected volume range.

Addressing Claims 2 and 16, it will be first noted that sample volume is only intended use. In any event, a sample volume less than about 5 ml is implied by col. 7, ll. 12-17 of the Speicher et al. reference, which teaches each compartment having a volume of less than 5 ml. Again, it would have been obvious to scale the apparatus to accommodate a sample volume within the expected volume range.

Addressing Claims 3 and 17, it will be first noted that sample volume is only intended use. In any event, a sample volume within the range of up to about 2 ml is implied by col. 7, ll. 12-17 of the Speicher et al. reference, which teaches each compartment having a volume of

preferably less than 2 ml. Again, it would have been obvious to one with ordinary skill in the art at the time of the invention to scale the apparatus to accommodate a sample volume within the expected volume range.

Addressing claims 4 and 18, The Murakawa et al. reference as modified by the Speicher et al. reference does not mention a sample volume within the range of up to about 0.02 ml to about 0.1 ml. It will be first noted that sample volume is only intended use. In any event, the Speicher et al. reference teaches the compartments each having a preferred volume of less than about 0.1 ml, which would include Applicant's claimed range. Furthermore, it would have been obvious to scale the apparatus to best accommodate a sample volume within the expected volume range.

Addressing claims 5-8 and 19-22, these claims only provide intended uses that do not structurally further limit the invention of claim 1. Since no specific sample volume, which is an intended use, is required by any of these claims, the barrier surface area is not limited. Thus, the rejection of claim 1, above, also applies to claims 5-8. Applicant should note that the Speicher et al. reference discloses a large range for the membrane area (col. 6, ll. 49-53).

Addressing claims 9, 10, and 24 as seen in col. 4, ln. 55 – col. 5, ln. 54, especially col. 5, ll. 44-46, the Speicher et al. reference discloses various separation barriers, which are electrophoresis membranes including a membrane made of polyacrylamide that is permeable to small ions and has a molecular weight cut-off of 1kDa. It would have been obvious to one with

ordinary skill in the art at the time the invention was made to use electrophoresis membranes with a molecular weight cut-off of 1 kDa as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference if molecules with a molecular weight of about 1 kDa are to be separated out because the molecular weight cut-off of the membrane should be the same as molecular desired molecular-weight separation threshold for the molecules.

Addressing claims 11 and 25, the Murakawa et al. reference teaches using membranes with different molecular weight cut-offs to separate larger molecules of interest from smaller molecules (abstract).

Addressing cliam 14, the Murakawa et al. reference also does not mention "a plurality of of separation barriers spaced apart defining a plurality of intersitial volumes" The Speicher et al. reference teaches providing a plurality of separation membranes (Figure 1). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide a plurality of separation membranes as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because then several separation compartments can be formed. Thus, the sample constituents can be then divided into several subgroups each limited in range along one separation property, rather than just one subgroup, so more selective partitioning of the sample constituents can be obtained. Indeed, the Murakawa et al. reference provides for at least two molecular-weight partitioning films (abstract).

Addressing claim 15, the Murakawa et al. reference teaches an apparatus for processing compounds (abstract and Fig. 1), by electrophoretic separation (abstract), the apparatus comprising:

(a) a cathode (**2** in Fig. 1) in a static cathode buffer zone;

(b) an anode (**3**) in a static anode buffer zone, the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode;

(c) a first separation barrier (**5**) disposed in the electric field area;

(d) a second separation barrier (**6**) disposed between a selected one of the cathode buffer zone and the anode buffer zone and the first barrier so as to define a first interstitial volume (**4**) therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone and the anode buffer zone, a sample constituent is provided to the first interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent through a selected one of the first and second separation barriers, and provided to a selected one of the cathode buffer and anode buffer zones; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones or the first interstitial volume (abstract and Fig. 1).

The Murakawa et al. reference does not mention whether the apparatus is configured for small sample volumes. The Speicher et al. reference teaches an apparatus for separating molecules using an electric field, the apparatus having an anode, a cathode, and several separation membranes and when used the apparatus does not circulate the anode buffer, the

cathode buffer, or sample constituents. The apparatus of the Speicher et al. reference is clearly configured for small sample volumes as the reference teaches compartments formed by separation membranes each having a volume of less than 5 ml. It would have been obvious to one with ordinary skill in the art at the time the invention was made to scale the apparatus to process a small sample volume as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because this will optimize the apparatus for separations on small sample volumes. In other words, it would have been obvious to scale the apparatus to accommodate a sample volume within the expected volume range.

The Murakawa et al. reference also does not mention "a third separation barrier disposed between the anode buffer zone and the first barrier so as to define a second interstitial volume therebetween." The Speicher et al. reference teaches providing a third separation membrane (Figure 1). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide a third membrane as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because then several separation compartments can be formed. Thus, the sample constituents can be then divided into several subgroups each limited in range along one separation property, rather than just one subgroup, so more selective partitioning of the sample constituents can be obtained. Indeed, the Murakawa et al. reference provides for at least two molecular-weight partitioning films (abstract).

Addressing claim 23, at least one membrane having a defined pore size is implied by the abstract of the Murakawa et al. reference, which teaches one membrane having a larger

molecular weight cutoff than another membrane. That other membranes are permeable to ions under an electric field is implied since the membranes are permeable to molecules.

Addressing claim 28, the Murakawa et al. reference teaches an apparatus for processing compounds (abstract and Fig. 1), by electrophoretic separation (abstract), the apparatus comprising:

(a) a cathode (**2** in Fig. 1) in a static cathode buffer zone;

(b) an anode (**3**) in a static anode buffer zone, the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode;

(c) a first separation barrier (**5**) disposed in the electric field area;

(d) a second separation barrier (**6**) disposed between the cathode buffer zone and the first barrier so as to define a first sample interstitial volume (**4**) therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone and the anode buffer zone, and the first sample interstitial volume, a sample constituent is provided to the first interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent through the first separation barrier, and; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones or the first sample interstitial volume (abstract and Fig. 1).

The Murakawa et al. reference does not mention whether the apparatus is configured for small sample volumes. The Speicher et al. reference teaches an apparatus for separating molecules using an electric field, the apparatus having an anode, a cathode, and several

separation membranes and when used the apparatus does not circulate the anode buffer, the cathode buffer, or sample constituents. The apparatus of the Speicher et al. reference is clearly configured for small sample volumes as the reference teaches compartments formed by separation membranes each having a volume of less than 5 ml. It would have been obvious to one with ordinary skill in the art at the time the invention was made to scale the apparatus to process a small sample volume as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because this will optimize the apparatus for separations on small sample volumes. In other words, it would have been obvious to scale the apparatus to accommodate a sample volume within the expected volume range.

The Murakawa et al. reference also does not mention "a third separation barrier disposed between the anode buffer zone and the first barrier so as to define a first separation interstitial volume therebetween." The Speicher et al. reference teaches providing a third separation membrane (Figure 1). It would have been obvious to one with ordinary skill in the art at the time the invention was made to provide a third membrane as taught by the Speicher et al. reference in the invention of the Murakawa et al. reference because then several separation compartments can be formed. Thus, the sample constituents can be then divided into several subgroups each limited in range along one separation property, rather than just one subgroup, so more selective partitioning of the sample constituents can be obtained. Indeed, the Murakawa et al. reference provides for at least two molecular-weight partitioning films.

Addressing claims 29, 30, and 32 as stated in the rejection of claim 28, the Murakawa et al. reference provides for at least two molecular-weight partitioning films. Barring evidence to the contrary, such as unexpected results, the number of separation barriers will depend on the

number of compartments desired; that is, on the number of subgroups into which the sample constituents is to be divided.

Addressing claim 31, a second cathode and a second anode as claimed is just mere duplication of parts. It would have been obvious to one with ordinary skill in the art at the time of the invention to provide a second cathode and a second anode as claimed because then two samples may be simultaneously separated by electrophoresis in independent electrophoresis units. Note that Applicant's claim language does not require electrophoresis units with shared membranes as in Figure 6, but reads on two independent electrophoresis units as in Figure 3.

Addressing claims 35 and 36, separating a compound in small volumes of solution is taught in the abstract. The claim steps of adding anode and cathode buffer, introducing a sample into the apparatus, and applying a voltage potential are clearly necessary in order to use the apparatus for separating a compound in a sample volume.

11. Claims 4, 18, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Speicher et al. (US 6,638,408 B1).

Addressing claim 4, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (abstract and col. 7, ll. 12-17, which teaches each compartment

having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between a selected one of the cathode buffer zone and the anode buffer zone and the first barrier so as to define a first interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone and the anode buffer zone, a sample constituent is provided to the first interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent through a selected one of the first and second separation barriers, and provided to a selected one of the cathode buffer and anode buffer zones; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones or the first interstitial volume (anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

The Speicher et al. reference does not mention a sample volume within the range of up to about 0.02 ml to about 0.1 ml. It will be first noted that sample volume is only intended use, which does not structurally modify the apparatus. In any event, the claimed sample volume range is *prima facie* obvious because the Speicher et al. reference teaches the compartments each having a preferred volume of less than about 0.1 ml, which would include Applicant's claimed range. Furthermore, it would have been obvious to one with ordinary skill in the art at the time of the invention to scale the apparatus to best accommodate a sample volume within the expected volume range.

Addressing claim 18, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (abstract and col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between the cathode buffer zone and the first barrier so as to define a first interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

(e) a third separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first or second separation barrier) disposed between the anode buffer zone and the first barrier so as to define a second interstitial volume therebetween;

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone, the anode buffer zone, and at least one of the first interstitial and second interstitial volumes, a sample constituent is provided to a selected one of the first interstitial and second interstitial volumes, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent, through the first separation barrier, and provided to a selected one of the cathode buffer and anode buffer zones; and provided to the other of the first interstitial and second interstitial volumes; and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones, the first interstitial volume or the second interstitial volume (anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

The Speicher et al. reference does not mention a sample volume within the range of up to about 0.02 ml to about 0.1 ml. It will be first noted that sample volume is only intended use, which does not structurally modify the apparatus. In any event, the claimed sample volume range is *prima facie* obvious because the Speicher et al. reference teaches the compartments each having a preferred volume of less than about 0.1 ml, which would include Applicant's claimed range. Furthermore, it would have been obvious to one with ordinary skill in the art at the time of the invention to scale the apparatus to best accommodate a sample volume within the expected volume range.

Addressing claim 31, the Speicher et al. reference teaches an apparatus for processing compounds in small volumes (abstract and col. 7, ll. 12-17, which teaches each compartment having a volume of less than 5 ml), by electrophoretic separation (implied by the abstract, which teaches using the apparatus for isoelectric focusing), the apparatus comprising:

(a) a cathode ("(-)" in Fig. 1) in a static cathode buffer zone (**170**);

(b) an anode ("(+)") in a static anode buffer zone (**210**), the anode disposed relative to the cathode so as to be adapted to generate an electric field in an electric field area therebetween upon application of a voltage potential between the cathode and anode (Fig. 1);

(c) a first separation barrier (**130**, **140**, **145**, **150**, or **160**) disposed in the electric field area;

(d) a second separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first separation barrier) disposed between the cathode buffer zone and the first barrier so as to define a first sample interstitial volume (**180**, **185**, **190**, **195**, or **200**) therebetween;

(e) a third separation barrier (any of **130**, **140**, **145**, **150**, or **160** not selected as the first or second separation barrier) disposed between the anode buffer zone and the first barrier so as to define a first separation interstitial volume therebetween (any of **180**, **185**, **190**, **195**, or **200** not selected as the first sample interstitial volume);

wherein in use, electrophoretic buffer is disposed in the cathode buffer zone, the anode buffer zone, and at least one of the first sample interstitial and first separation interstitial volumes, a sample constituent is provided to a selected one of the first sample interstitial volume, wherein upon application of the voltage potential, a selected separation product is removed from the sample constituent, through the first separation barrier, and

provided to the first separation interstitial volume, and wherein there is substantially no circulation of buffer or sample constituent in the buffer zones, the first interstitial volume or the first separation interstitial volume (anode and cathode buffers are disclosed in col. 5, ll. 7-17, for example. As seen from Figure 1 neither buffer nor sample constituents are circulated. Elements **230** are optional access ports).

Note that at least a fourth separation barrier is shown in Figure 1.

A second cathode and a second anode as claimed is just mere duplication of parts. It would have been obvious to one with ordinary skill in the art at the time of the invention to provide a second cathode and a second anode as claimed because then two samples may be simultaneously separated by electrophoresis in independent electrophoresis units. Note that Applicant's claim language does not require electrophoresis units with shared membranes as in Figure 6, but reads on two independent electrophoresis units as in Figure 3.

Allowable Subject Matter

12. Claims 33 and 34 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

13. The following is a statement of reasons for the indication of allowable subject matter:

a) Claims 33 and 34 each require at least one compound to be retained in an interstitial volume and selected salts in the sample to be removed into either the cathode buffer zone

or the anode buffer zone. Although the Speicher et al. reference and the Murakawa et al. reference teach retaining at least one compound in an interstitial volume neither teaches selectively removing a salt as claimed;

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (703) 305-5686. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (703) 308-3322. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Alex Noguerola
Alex Noguérola
11/07/03
Primary Examiner
TC1753